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(57) Abstract

A process and catalyst composition are provided for the highly efficient enantioselective hydrogenation of dehydroamino acid derivatives. The catalyst composition comprises rhodium or iridium and a diphosphinite carbohydrate ligand, wherein the phosphorous atoms are attached to aromatic groups substituted with electron-donating substituents. Also provided is a means to selectively produce α amino acids in either the L or the D form, based upon use of a sugar in the ligand with phosphinites attached in an absolute Right-Left or Left-Right configuration, respectively.

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TITLE

SELECTIVE ASYMMETRIC HYDROGENATION OF DEHYDROAMINO ACID DERIVATIVES USING RHODIUM AND IRIDIUM DIPHOSPHINITE CARBOHYDRATE CATALYST COMPOSITIONS

FIELD OF THE INVENTION

This invention relates to a process and catalyst composition for the asymmetric hydrogenation of dehydroamino acid derivatives to selectively produce either D or L amino acid compounds. The process utilizes a catalyst composition comprising rhodium or iridium and a diphosphinite carbohydrate ligand, wherein the ordered absolute configuration of the two phosphinite groups on the carbohydrate determines whether the α amino acids produced will be D or L. Further, the ligands of the invention comprising phosphinite groups which have aromatic groups substituted with electron-donating substituents, result in catalysts which display very efficient enantioselectivity during the hydrogenation reaction.

BACKGROUND OF THE INVENTION

The subject of asymmetric hydrogenation, especially using dehydroamino acid derivatives as substrates, is a commercially important area, particularly in the pharmaceutical field.

Cullen reported the use of the 2,3-glucopyranose system for asymmetric hydrogenation of dehydroamino acid derivatives in 1978 (Tetrahedron Lett. **1978**, 1635). Similar disclosures were made by Thompson (J. Organometal. Chem. **1978**, 159, C29; U.K. 41,806,177 7/10/77).

Jackson and Thompson (*J. Organomet. Chem.* **1978**, *159* , C29) describe the use of 2,3-diphenylphosphinites of a "D-glucopyranose" for S-phenylalanine and 4,6-diphenylphosphinite of a "D-xylofuranose" for the corresponding R amino acid. Thus, unlike the present invention, in order to make R and S amino acid derivatives altogether *different* sugar back bones were previously employed. Habus, Raza and Sunjic (*J. Mol. Cata.* **1987**, *42*, 173) also report similar results using "D-glucopyranose" and "D-xylopyranose"-derived bis-diphenylphosphinites for the synthesis of R and S-phenylalanine derivatives. The enantioselectivity in each case is low and in contrast to the present invention, reaction conditions are not practical for large scale preparation of these compounds, where high selectivity is needed.

Selke et al. began work in this area in 1978 and has published a series of papers and also patented some of this work. (*J. Mol. Catal.* **1986**, *37*, 213,227;

J. Prakt. Chem. **1987**, *329*(4), 717; *J. Mol. Catal.* **1989**, *56*, 315; DD 140 036; DD 240 372; and DD 248 028). Similar to Cullen and Thompson, Selke discloses using a phenyl group on the phosphorus. Unlike Applicants' process, however, the phosphorus phenyl group was unsubstituted and no recognition was disclosed of enhanced enantioselectivity as a function of electron-rich substituents on the phenyl. Further, the Selke, Cullen and Thompson disclosures are limited to ligands using "2,3-dideoxyglucopyranose", "mannopyranose" and "galactopyranose" in systems yielding only S amino acid derivatives.

Other sugar diphosphinites have been examined in both rhodium (J. Org. Chem. **1980**, 45, 62) and ruthenium (J. Mol. Catal. **1980**, 9, 307) catalyzed hydrogenation reactions. However, low ee's were obtained. Some simple derivatives have also been reported by Sunjic (Sunjic: J. Mol. Catal. **1987**, 42, 173); again, in processes yielding low ee values.

Other references disclose carbohydrates as the chiral auxiliary for monophosphinites (Yamashita: Carbohydrate Res. **1981**, 95 C9; Bull. Chem. Soc. Jpn. **1982**, 55, 2917; Bull. Chem. Soc. Jpn. **1986**, 59, 175) and phosphines (Sunjic: J. Organometal. Chem. **1989**, 370, 295; Nakamura: Chem. Lett. **1980**, 7).

Aminophoshine-phosphinites from readily available amino acids have also been used as ligands for asymmetric hydrogenations. (U.S. Patent 5,099,077, 3/24/1992; Petit, M.; Mortreaux, A.; Petit, F.; Buono, G.; Peiffer, G. *Nou. J. Chem.* **1983**, 593.)

SUMMARY OF THE INVENTION

The present invention provides a process for asymmetric hydrogenation, comprising:

reacting a dehydroamino acid derivative of formula I

$$ZZC{=}C(CO_2Z)(NHZ)$$

I

wherein each Z is independently H or a C_1 to C_{40} carboalkoxy, C_1 to C_{40} aromatic or nonaromatic hydrocarbyl or C_1 to C_{40} aromatic or nonaromatic heterocyclic radical; optionally substituted with one or more halo, alkoxy, carboalkoxy, nitro, haloalkyl, hydroxy, amido, keto, or sulfur containing groups;

with a source of hydrogen;

in the presence of a catalyst composition comprising iridium or rhodium and a chiral, nonracemic diphosphinite ligand of formula II

$$(R^1)_2\text{-P-X-}R^2\text{-X-P-}(R^1)_2$$

II

wherein R^2 is a C_4 to C_{40} dideoxycarbohydrate;

each X is independently O or NR^3, wherein R^3 is H, a C_1 to C_{20} alkyl or aryl; and

each R^1 is independently an aromatic hydrocarbyl substituted with one or more amino, dialkylamino, hydroxy, alkoxy, alkyl, triarylsilyl, or trialkylsilyl groups, or an aromatic heterocycle substituted with one or more amino, dialkylamino, hydroxy, alkoxy, alkyl, trialkylsilyl, or triarylsilyl groups;

to yield a chiral, nonracemic mixture of compounds of formula III

$$ZZCH\text{-}CH(CO_2Z)(NHZ)$$

III

wherein Z is defined as above.

This invention further provides a method for predicting whether the above hydrogenation process will yield an R or S amino acid derivative, based upon whether the absolute configuration of the phosphinite groups "X" attached to the carbohydrate R^2 are configured in Right-Left configuration to yield the S amino acid derivation of Formula III, or are configured in a Left-Right configuration to yield the R amino acid derivative of Formula III.

This invention further provides a catalyst composition comprising iridium or rhodium and a chiral, nonracemic diphosphinite ligand of formula II

$$(R^1)_2\text{-P-X-}R^2\text{-X-P-}(R^1)_2$$

II

wherein R^2 is a C_4 to C_{40} dideoxycarbohydrate;

each X is independently O or NR^3, wherein R^3 is H, a C_1 to C_{20} alkyl or aryl; and

each R^1 is independently an aromatic hydrocarbyl substituted with amino, dialkylamino, hydroxy, alkoxy, alkyl, trialkylsilyl, or triarylsilyl groups or

an aromatic heterocycle substituted with amino, dialkylamino, hydroxy, alkoxy, alkyl, trialkylsilyl, or triarylsilyl groups.

This invention further provides a process for asymmetric hydrogenation, comprising reacting a dehydroamino acid derivative of formula I

$$ZZC=C(CO_2Z)(NHZ)$$

I

wherein each Z is independently H or a C_1 to C_{40} carboalkoxy, C_1 to C_{40} aromatic or nonaromatic hydrocarbyl or C_1 to C_{40} aromatic or nonaromatic heterocyclic radical, optionally substituted with one or more halo, alkoxy, carboalkoxy, nitro, haloalkyl, hydroxy, amido, keto or sulfur containing groups;

with a source of hydrogen;

in the presence of a catalyst composition comprising iridium or rhodium and a chiral nonracemic diphosphinite ligand of formula II

$$(R^1)_2\text{-P-X-}R^2\text{-X-P-}(R^1)_2$$

II

wherein R^2 is a C_4 to C_{40} dideoxycarbohydrate;

each X is independently O or NR^3, wherein R^3 is H, a C_1 to C_{20} alkyl or aryl; and

each R^1 is an unsubstituted aromatic hydrocarbyl,

to yield a chiral, nonracemic mixture of compounds of formula III

$$ZZCH\text{-}CH(CO_2Z)(NHZ)$$

III

wherein Z is defined as above;

and wherein in formula II the X groups are attached to R^2 in the Left-Right diphosphinite configuration whereby the asymmetric hydrogenation process selectively yields compounds of formula III in R-configuration.

DETAILED DESCRIPTION OF THE INVENTION

The process and catalyst composition of the instant invention whereby enantioselective hydrogenation is accomplished by reacting a dehydroamino acid

derivative of the formula ZZC=C(CO_2Z)(NHZ) with hydrogen in the presence of a chiral, nonracemic, metal (Rh, Ir) hydrogenation catalyst, are useful, for example to produce optically active amino acid derivatives. These amino acid derivatives are useful precursors for pharmaceutical products.

The enantioselective hydrogenation reaction is performed by reacting a dehydroamino acid derivative of the formula ZZC=C(CO_2Z)(NHZ) with hydrogen in the presence of a chiral, nonracemic, metal (Rh, Ir) hydrogenation catalyst. These reactions selectively provide optically active D or L -α- amino acid derivatives of the formula ZZCHCH(CO_2Z)(NHZ), where the absolute configuration of the amino acid derivative is determined by the nature of the chiral metal hydrogenation catalyst.

By the term "carbohydrate", Applicants mean the class of organic compounds comprising the general formula $(CH_2O)_n$, wherein n is equal to or greater than four. The carbohydrate-derived ligands of the invention are derived from C_4 to C_{40} carbohydrates including monosaccharides, disaccharides and oligosaccharides.

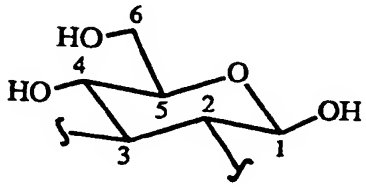
By the term "hydrocarbyl", Applicants include all alkyl, aryl, aralkyl or alkylaryl carbon substituents, either straight-chained, cyclic, or branched, accordingly substituted with hydrogen.

By the term "heterocycle", Applicants mean a cyclic carbon compound containing at least one oxygen, nitrogen or sulfur atom in the ring.

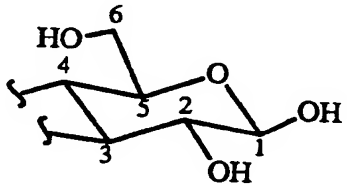
By the term electron-donating group, Applicants include those groups that have σ-values (any σ-values such as σ_p, σ_m or their modifications) less than zero (as defined by the Hammett equation, see, for example, March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 4th ed.; 1992, Wiley: New York, 278-286). Such groups include but are not limited to O^-, NMe_2, NH_2, OH, OMe, CMe_3, Me, Me_3Si, SMe, and F.

In describing a carbohydrate group of the formula X-R^2-X, the "X" can be the same or different and can be O or NR^3, where R^3 is H, alkyl or aryl; and as it appears within the ligand of the present disclosure, the group R^2 is named by using the prefix "dideoxy" with the name of the parent diol of the formula HO-R^2-OH. The suffix "pyranose" or "furanose" in combination with the carbohydrate root names shall include those compounds wherein the sugar exists as an internal 6- (pyranose) or 5- (furanose) membered acetal. The OH groups may or may not be

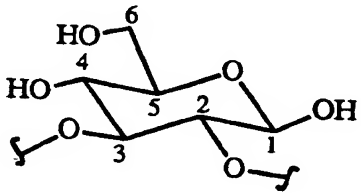
protected as esters or ethers. For example, the name "2,3-dideoxy-glucopyranose" refers to the group:



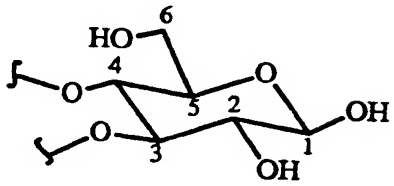
and "3,4-dideoxy-glucopyranose" refers to the group:



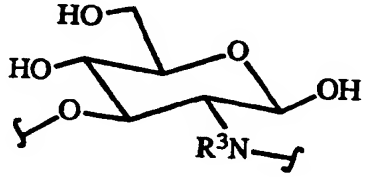
Accordingly, the corresponding carbohydrate groups O-R^2-O are:



and



Nitrogen may be substituted for one or both of the oxygens in the above formula O-R^2-O to provide an aminosugar. An example of the carbohydrate group O-R^2-NR^3 is the "2,3-dideoxyglucose":



The suffix -ose- when used in combination with carbohydrate root names, shall include those compounds wherein the OH groups are protected as ethers or esters. By this definition, for example, the pyranoside structure shown below is termed a "glucopyranose" since the configuration of the sugar back-bone (C_1-C_5) is that of the sugar glucose,

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der nach Regel 45 des Europäischen Patentübereinkommens für das weitere Verfahren als europäischer Recherchenbericht gilt

Nummer der Anmeldung: EP 03 01 9803

EINSCHLÄGIGE DOKUMENTE

Kategorie	Kennzeichnung des Dokuments mit Angabe, soweit erforderlich der maßgeblichen Teile	Betrifft Anspruch	KLASSIFIKATION DER ANMELDUNG (Int.Cl.7)
A	WO 96 16971 A (LONZA AG ;BRIEDEN WALTER (CH)) 6. Juni 1996 (1996-06-06) Formel Ia * das ganze Dokument *	1	C07F9/655
A	EP 0 885 897 A (BASF AKTIENGESELLSCHAFT, GERMANY) 23. Dezember 1998 (1998-12-23) * Beispiel 3 *	1-8	
A	* Seite 5, Zeile 25 - Seite 6, Zeile 1 *	9-25	
A	RAJANBABU, T. V. ET AL: "Carbohydrate Phosphinites as Practical Ligands in Asymmetric Catalysis: Electronic Effects and Dependence of Backbone Chirality in Rh-Catalyzed Asymmetric Hydrogenations. Synthesis of R- or S-Amino Acids Using Natural Sugars as Ligand Precursors" JOURNAL OF ORGANIC CHEMISTRY (1997), 62(17), 6012-6028 , XP002216106 Seite 6026, Spalte 2; Verbindung 31 * Seite 6015 - Seite 6020; Abbildung 3; Tabelle 4 *	1-25 Prev. Sub.	
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RECHERCHIERTE SACHGEBIETE (Int.Cl.7): C07F

UNVOLLSTÄNDIGE RECHERCHE

Die Recherchenabteilung ist der Auffassung, daß ein oder mehrere Ansprüche, den Vorschriften des EPÜ in einem solchen Umfang nicht entspricht bzw. entsprechen, daß sinnvolle Ermittlungen über den Stand der Technik für diese Ansprüche nicht, bzw. nur teilweise, möglich sind.

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Grund für die Beschränkung der Recherche:

Siehe Ergänzungsblatt C

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Recherchenort	Abschlußdatum der Recherche	Prüfer
MÜNCHEN	20. November 2003	Richter, H

KATEGORIE DER GENANNTEN DOKUMENTEN

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EPO FORM 1503 03.82 (P04C09)

EINSCHLÄGIGE DOKUMENTE			KLASSIFIKATION DER ANMELDUNG (Int.Cl.7)
Kategorie	Kennzeichnung des Dokuments mit Angabe, soweit erforderlich der maßgeblichen Teile	Betrifft Anspruch	
A	RAJANBABU, T. V. ET AL: "Role of Electronic Asymmetry in the Design of New Ligands: The Asymmetric Hydrocyanation Reaction" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY (1996), 118(26), 6325-6326 , XP002262100 * das ganze Dokument * ---	1-25	
A	WO 95 18787 A (DU PONT DE NEMOURS, E. I., AND CO., USA) 13. Juli 1995 (1995-07-13) Seite 12 * Seite 27, Zeile 11 - Seite 30; Tabelle 1 * ---	1-25	RECHERCHIERTE SACHGEBIETE (Int.Cl.7)
A	CHEMICAL ABSTRACTS, vol. 72, no. 17, 27. April 1970 (1970-04-27) Columbus, Ohio, US; abstract no. 90791, HOLY, ANTONIN: "Nucleic acid components and their analogs. CXXX. Preparation of nucleotide derivatives of 1'-homouridine and their behavior towards some nucleolytic enzymes" XP002262101 Verbindung I * Zusammenfassung * & COLLECTION OF CZECHOSLOVAK CHEMICAL COMMUNICATIONS (1970), 35(1), 81-8 , 1970, --- -/--	1-8	

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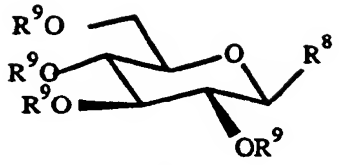


5

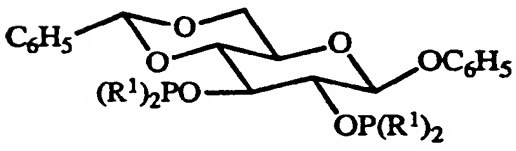
wherein:

R^8 is H, C_1 to C_{20} hydrocarbyl, alkoxy, or aryloxy;

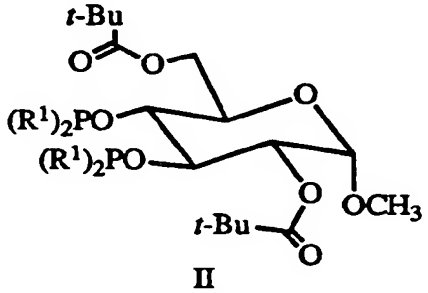
R^9 is independently selected from H, C_1 to C_{20} hydrocarbyl, acyl or $P(R^1)_2$, where R^1 is aryl, alkoxy, aryloxy;

and the sum total of $P(R^1)_2$ groups present in the O-substituted glucopyranose organophosphorus ligand is equal to 2.

Examples of the ligands used in the present invention include the following:



I



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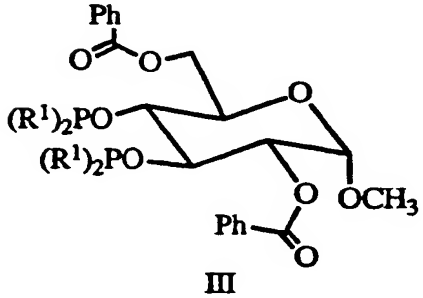

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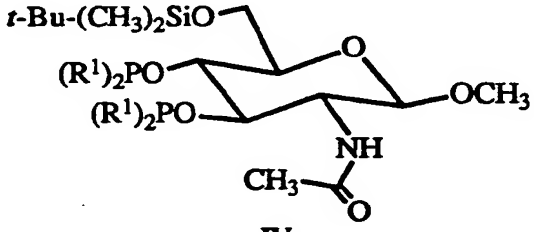

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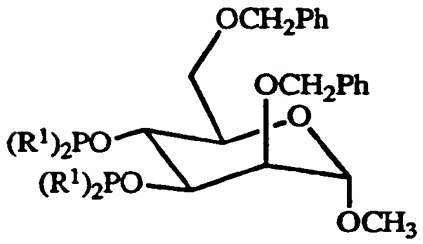

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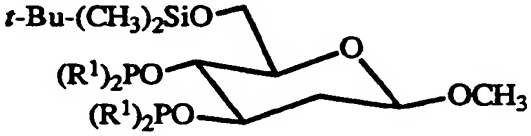

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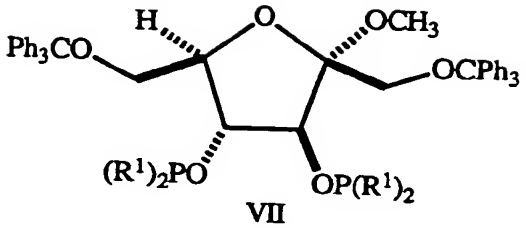

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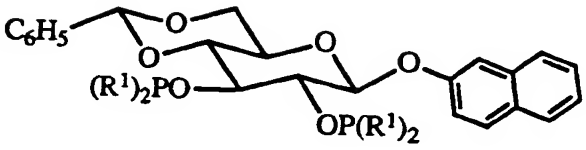


VIII

A. R^1=Ph
B. R^1=3,5-$(CH_3)_2C_6H_3$
C. R^1=4-$(CH_3O)C_6H_4$
D. R^1=4-FC_6H_4
E. R^1=3,5-$F_2C_6H_3$
F. R^1=3,5-$(CF_3)_2C_6H_3$
G. R^1=4-$(CF_3)C_6H_4$
H. R^1=3,5-$(CH_3)_2$-4-$(CH_3O)C_6H_2$
J. R^1,R^1=[R]-2,2'-Binaptholate

Using the above representation of the ligands, the catalysts are described as follows: [IA] $Rh(COD)SbF_6$ refers to a catalyst prepared from ligand IA and $Rh(COD)_2SbF_6$; [IIB] $Rh(COD)BF_4$ refers to a catalyst prepared from ligand IIB and $Rh(COD)_2BF_4$, etc.

For illustrative purpose, ligands IA, IB, IE and IF may be defined as follows in the context of the general definition (i.e., $(R^1)_2$-P-X-R^2-X-P-$(R^1)_2$) of the:

IA: R^2: "2,3-dideoxyglucopyranose" X = O, X = O; R^1 = Phenyl
IB: R^2: "2,3-dideoxyglucopyranose" X = O, X = O; R1 = 3,5-dimethylphenyl
IE: R^2: "2,3-dideoxyglucopyranose" X = O, X = O; R^1 = 3,5-difluorophenyl
IF: R^2: "2,3-dideoxyglucopyranose" X = O, X = O; R^1 = 3,5-bis(CF_3) phenyl

The ligands of the invention are defined to contain R^1 groups which are substituted with electron-donating groups. The beneficial electronic effect of these ligands can be illustrated by comparing ligands IA, IB, IE and IF in the Rh(+)-catalyzed hydrogenation of methyl 2-acetamido-3-(4-fluorophenyl)propen-2-oate. An 85% ee was obtained when diphenylphosphinite IA was used, whereas a 96% ee was obtained with the more electron rich 3,5-dimethylphenyl phosphinite IB. Very low ee's of 13% ad 9% were obtained using electron-deficient systems, 3,5-difluorophenylphosphinite IE and 3,5-bis-trifluoromethylphenyl-phosphinite IF, respectively. Applicants believe that utilization of this electronic effect will prove to be highly significant and beneficial in applications necessitating practical means of synthesis of amino acids in very high enantioselectivity.

Examples where high ee's were obtained for the Rh(+)-catalyzed hydrogenation of methyl 2-acetamidocinnamate include IB (*S*-99.0%), IIB (*R*-

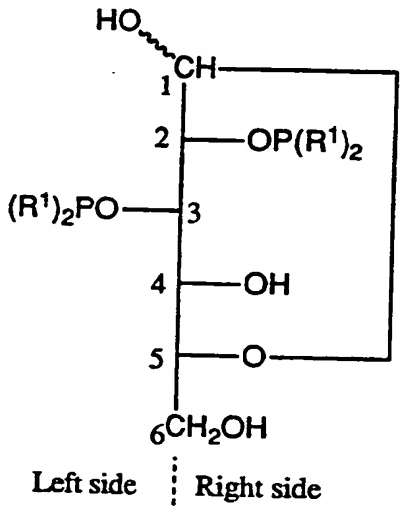
93.0%), IIIB (*R*-97.0%), and IVB (*R*-98.3%). The hydrogenation of other substrates are illustrated in the tables.

Another highly significant aspect of the present invention relates to Applicants' recognition that the relative regiochemistry of the vicinal-phosphinites with respect to their location on a given sugar back-bone ("glucose", for example) dictates which amino acid (R or S; or D or L) is generated in the hydrogenation. For example, *S*-amino acids are obtained when ligands I and VIII are used, whereas *R*-amino acids are obtained when ligands II, III or IV are used in the reduction of dehydroamino acid derivatives. For purposes of clarity and uniformity, Applicants have characterized and described this element of the invention in terms of the ordered absolute configurations of the phosphinites on sugar back-bone Fisher Projections. In this context, the ordered absolute configuration of the phosphinites on the sugar will be designated unambiguously as either Right-Left, or Left-Right. Applicants are the first to recognize that a Right-Left (occupying the 2,3-position of the sugar) ligand configuration results in formation of the S enantiomer or L amino acid, whereas the Left-Right ligand configuration (occupying the 3,4-position of the sugar) results in formation of the R enantiomer or D amino acid. More specifically, using Fisher Projections (see, for example, Stryer, L. Biochemistry, 3rd ed.; 1988, Freeman: New York, 332-336) of furanose and pyranose derived vicinal diphosphinites, the sense of chirality of products formed in the Rh-catalyzed hydrogenation of dehydroamino acid derivatives can be predicted. In doing so the configuration of the carbon with the lower number is indicated first. Thus, Right-Left diphosphinite indicates that the carbon carrying the right phosphinite is lower in number in the context of the Fisher Projection.

Pyranose and furanose sugars that have a Right-Left diphosphinite configuration (see text for convention) give L-amino acid derivatives (corresponding to S configurations) and those sugars with a Left-Right diphosphinite configuration give D-amino acid derivatives (corresponding to R configurations) when used in the Rh or Ir catalyzed hydrogenation of dehydro-amino acid derivatives.

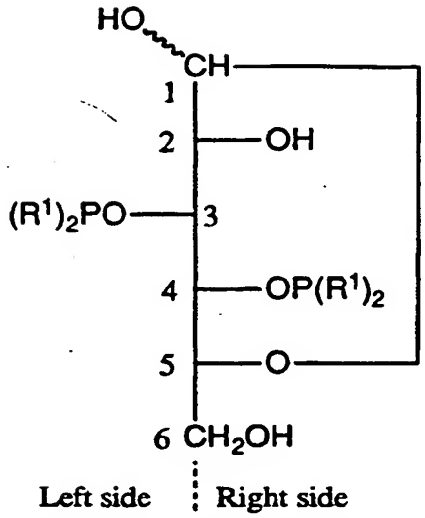
When the diphosphinites are on the 2,3-positions of D-glucose as shown, the product of the hydrogenation is a L-amino acid (S-configuration). Using Fisher Projections of the sugar derivatives, one can pictorially define the relative location of the diphosphinites on either the left or right side. In this way, by using the

standard numbering for carbohydrate nomenclature, the first phosphinite (on the 2-position) is on the right side and the second phosphinite (on the 3-position) is on the left side of the glucose systems. We are defining this as a Right-Left diphosphinite.



Right-Left diphosphinite from D-Glucose

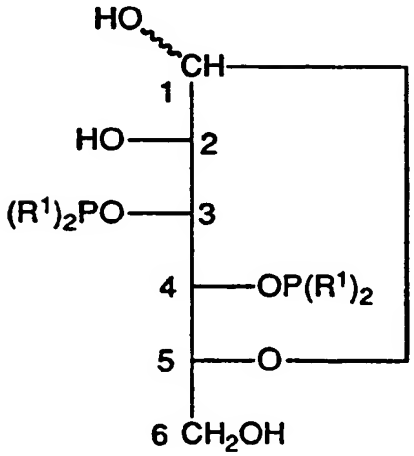
Accordingly, when diphosphinites are on the 3,4-positions of D-glucose as shown, the product of the hydrogenation is a D-amino acid (R-configuration). Once again using the standard numbering for carbohydrate nomenclature, the first phosphinite (on the 3-position) is on the left side and the second phosphinite (on the 4-position) is on the right side of the glucose systems. We are defining this as a Left-Right diphosphinite.



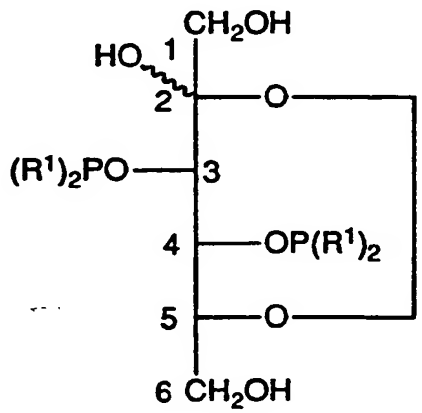
Left-Right diphosphinite from D-Glucose

Correspondingly, other sugar derivatives where a Right-Left diphosphinite is present will provide L-amino acids, whereas a Left-Right diphosphinite will provide D-amino acids when these ligands are used in the hydrogenation of dehydroamino acid derivatives.

Other examples enable us to further illustrate the understanding of this relationship of the sugar diphosphinites to the configuration of the product amino acid derivatives. The 3,4-diphosphinite derived from D-mannose and the 3,4-diphosphinite derived from D-fructose, both Left-Right diphosphinites provide D-amino acid derivatives under the hydrogenation conditions.

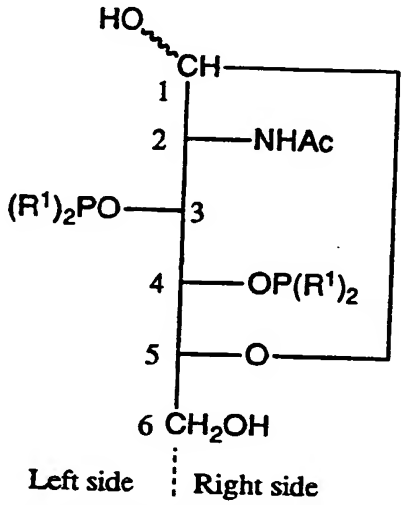


Left-Right diphosphinite from D-Mannose



Left-Right diphosphinite from D-Fructose

Also, the 2-deoxy-2-acetamido glucose derivative shown below is a Left-Right diphosphinite and provides D-amino acids under the hydrogenation conditions



Left-Right diphosphinite from D-Glucose

Within the context of the ligand formula II $(R^1)_2$-P-X-R^2-X-P-$(R^1)_2$ and the ligand nomenclature developed above, the ligands **IB**, **IIIB** and **IVB** may be compared in the process of the invention to further illustrate this configurational effect:

IB: R^2: "2,3-dideoxyglucopyranose" X = O, X = O; R^1 = 3,5-dimethylphenyl

IIIB: R^2: "3,4-dideoxyglucopyranose" X = O, X = O; R^1 = 3,5-dimethylphenyl

IVB: R^2: "3,4-dideoxyglucopyranose" X = O, X = O; R^1 = 3,5-dimethylphenyl

When R^1 = bis-(2,3-dimethylphenyl)phosphino, ligand **IB** serves as an efficient ligand for Rh(+) in the catalytic hydrogenation of methyl acetamido-cinnamate which is reduced to the corresponding S(+) methyl phenylalaninate in 99.0% ee. Under identical conditions, 93.0 and 98.3% ee of the R(-) isomer are obtained using ligand **IIIB** and **IVB**, respectively.

The configurationally specific chiral, nonracemic carbohydrate-derived diphosphorus ligands can be prepared according to techniques well-known in the art. (Selke, R.; Facklam, C.; Foken, H.; Heller, D. *Tetrahedron Asymmetry* **1993**, *4*, 369; Baker, M. J.; Pringle, P. G.; *J. Chem. Soc. Commun.* **1991**, 1292; Habus, I.; Raza, Z; Sunjic, V. *J. Mol. Catal.* **1987**, *42*, 173.; Jackson, W. R.; Lovel, C. G. *Aust. J. Chem.* **1982**, *35*, 2069; Jackson, R.; Thompson, D. J.

J. Organomet. Chem. **1978**, *159*, C29; Cullen, W. R.; Sugi, Y.; *Tetrahedron Lett.* **1978**, 1635). In general, diol derivatives containing unprotected hydroxyl groups are treated with a $P(R)_2Cl$ (wherein R may generally be an alkyl, aryl, alkoxy, or aryloxy) reagent, in the presence of a base, such as pyridine or triethylamine, to produce the desired phosphinite or phosphite. Some $P(R)_2Cl$ reagents are commercially available, such as PPh_2Cl (Ph = phenyl). Other $P(R)_2Cl$ reagents, where R = aryl or alkyl, can be prepared by two methods. Method A involves the reaction of (amino)dichlorophosphines such as Et_2NPCl_2 with RMgBr followed by reaction with HCl [Methoden Der Organischen Chemie (Houben-Weyl): Vol 12, Part 1; Muller, E., ed.; Georg Theme Verlag: Stuggart, 1963, 213-215; de Koe, P.; Bickelhaupt, F. *Angew. Chem. Int. Ed., Eng.* **1967**, *6*, 567; Quin, L. D.; Anderson, H. G. *J. Org. Chem.* **1966**, *31*, 1206.; Montgomery, R. E.; Quin, L. D. *J. Org. Chem.* **1965**, *30*, 2393; Frank, A. *J. Org. Chem.* **1961**, *26*, 850]. Alternatively, treatment of readily available dialkyl phosphites, such as dibutyl phosphite, $HP(O)(OBu)_2$, with RMgBr followed by reaction with PCl_3 provides $P(R)_2Cl$ derivatives (U.S. Patent 5,175,335). $P(R)_2Cl$ reagents, where R = alkoxy or aryloxy, can be prepared in two steps by treatment of $P(NEt_2)_3$ with ROH to generate $P(OR)_2(NEt_2)$, followed by treatment with CH_3COCl to generate $P(OR)_2Cl$. Illustrative preparations are provided below.

For all embodiments of the invention the chiral, nonracemic metal hydrogenation catalyst may be prepared by mixing the metal source and the chiral, nonracemic, organophosphorus ligand, preferably in a suitable organic solvent under an inert atmosphere such as N_2 or Ar in a temperature range from 0°C to 120°C, preferably in a temperature range from 0°C to 80°C. The metal compound may be used in this solution or the metal compound can be obtained in the pure form upon removal of the solvent. Rh is the preferred metal. Counter ions BF_4 and SBF_6 are preferred.

The preferred molar ratio of chiral, nonracemic, organophosphorus ligand to the metal may vary between 1:1 to 2:1, most preferably between 1:1 to 1.2:1.

The preferred molar ratio of metal complex to vinyl compound may vary between 0.00005:1 to 1:1, most preferably between 0.0001:1 to 0.01:1.

The dehydroamino acid derivative, represented by the formula $ZZC{=}C(CO_2Z)(NHZ)$ may be dissolved in any organic solvent such as, but not limited to, tetrahydrofuran, methanol, ethanol, dimethoxyethane, toluene or hexane.

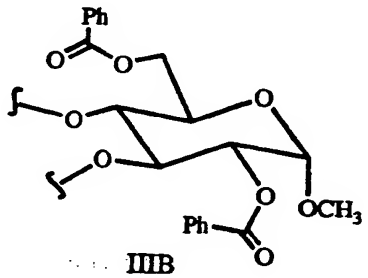
Tetrahydrofuran (THF), methanol, ethanol and dimethoxyethane and mixtures thereof are preferred solvents. THF is the most preferred.

The hydrogen can be provided by contacting the reaction mixture with hydrogen gas.

The hydrogenation reaction is preferably conducted over a temperature range from -25°C to 100°C, most preferably 25 to 30°C. Applicants note that higher ee's are observed at lower temperatures. Suitable pressure range is 10-100 psi (1 psi = 6.9 kPa).

The enantioselective hydrogenation reactions are typically complete within 3-24 hours.

To demonstrate a preferred mode of the invention which produces a particularly useful product, preparation of optically active (R)-(+)-phenylalanine can be achieved. The catalyst composition comprises a cationic rhodium (I) compound and the ligand formula $(R^1)_2P\text{-}X\text{-}R^2\text{-}XP(R^1)_2$ wherein each R^1 is the aryl group 3,5-dimethylphenyl and R^2 is the O-substituted β-D-glucopyranose of the formula IIIB, the starting acrylate derivative is α-acetamidocinnamic acid, and the source of rhodium metal is $(COD)_2RhSbF_6$.



IIIB

For the preparation of (R)-(+)-phenylalanine, the enantioselective hydrogenation is preferably carried out at 25°C under 40 psi pressure of hydrogen. A mixture of α-acetamidocinnamic acid and the chiral rhodium catalyst is stirred in a suitable solvent such as THF, DME, or CH_3OH for 3 h. In this preferred embodiment, a molar ratio between 0.0025:1 to 0.05:1 of rhodium catalyst to acrylate derivative is used.

Using these preferred conditions, ee's greater than 95% are typically obtained. Isolation of the product amino acid in 90-100% yield can be achieved by crystallization from the reaction mixture.

General Procedures for the Preparation of Chiral Carbohydrate Diols, Phosphinite Ligands $(R^1)_2P\text{-}X\text{-}R_2\text{-}X\text{-}P(R^1)2$ and Rh and Ir Catalysts Derived Therefrom

A. Synthesis of Diols

The requisite diols for the ligand synthesis (see Table 1) were prepared by procedures outlined below.

Phenyl 4,6-O-benzylidene-β-D-glucopyranoside. The title compound was prepared by treatment of commercially available phenyl-β-D-glucopyranoside with dimethoxytoluene in the presence of p-toluenesulfonic acid in acetonitrile (for leading references see Carbohydrates, Ed. Collins, P. M., Chapman and Hall, New York, 1987, 414).

Methyl 2,6-di-O-pivaloyl-α-D-glucopyranoside and Methyl 2,6-di-O-benzoyl-α-D-glucopyranoside. The requisite carbohydrate diols were synthesized according to literature procedures: (Ogawa, T.; Matsui, M. *Tetrahedron* **1981**, *37*, 2369; Tomic-Kulenovic, S.; Keglevic, D. *Carbohydrate Res.* **1980**, *85*, 302.).

Methyl 2-acetamido-2-deoxy-6-O-t-butyldimethylsilyl-β-D-glucopyranoside. This compound was prepared from the corresponding methyl glucoside, *Methyl 2-acetamido-2-deoxy-β-D-glucopyranoside* (Carbohydrates, Ed. Collins, P. M., Chapman and Hall, New York, 1987, p. 414) by treatment with *t*-butyldimethylchlorosilane in DMF and imidazole. ^{1}H NMR δ 0.00 (2Xs, 6 H), 0.80 (2Xs, 9 H), 1.98 (s, br, 3H), 3.20-3.32 (m, 1 H), 3.32-3.50 (s superimposed on m 5 H), 3.59 (dd, J = 12, 8, 1 H), 3.76, 3.84 (ABX, JAB = 18, 2 H), 4.28 (d, J = 8, 1 H), 6.42 (d br J = 4, 3 H).

Methyl 2-deoxy-6-O-t-butyldimethyl-α-D-glucopyranoside. This compound was prepared from the corresponding methyl glucoside, *Methyl 2-deoxy-α-D-glucopyranoside*. (Carbohydrates, Ed. Collins, P. M., Chapman and Hall, New York, 1987, p. 352) by treatment with *t*-butyldimethylchlorosilane in DMF and imidazole. ^{1}H NMR δ 4.73 (d, 1, J = 3 Hz), 3.85-3.78 (m, 4), 3.55-3.46 (m, 2), 3.35 (m, 1), 3.29 (s, 3), 2.05 (m, 1), 1.61 (m, 1), 0.88 (m, 9), 0.07 (m, 6).

Methyl 2,6-di-O-benzyl-α-D-mannopyranoside. A ca. 2:1 mixture of exo- and endo-isomers of bis-[(2,3-O-), (4,6-O-)] benzylidene-α-D-mannopyranoside (Carbohydrates, Ed. Collins, P. M., Chapman and Hall, New York, 1987, p. 350) was prepared by reaction of methyl α-D-mannopyranoside with 2.2 eq of α,α-dimethoxytoluene and catalytic p-toluenesulfonic acid in acetonitrile. This compound was treated with $NaBH_4$ and HCl (Garegg, P. J.; Hultberg, H.

Carbohydrate Res. **1981**, *93*, C10) to provide a mixture of products from which the methyl 2,6-O-benzyl-α-D-mannopyranoside was isolated by flash chromatography. The assignment of this isomer was confirmed by ^1H decoupling experiments on the corresponding bis-(3,4-O-diphenylphosphino) derivative (ligand VA). ^1H NMR δ 7.42-7.24 (m, 10), 4.81 (d, 1, J = 1 Hz), 4.75-4.54 (m, 4), 3.78-3.71 (m, 6), 3.36 (s, 3), 2.83 (bs, 1), 2.43 (bs, 1).

Methyl 1,6-O-trityl-α-D-fructofuranoside. The starting diol was prepared by tritylation of Methyl -α-D-fructofuranoside. (Carbohydrates, Ed. Collins, P. M., Chapman and Hall, New York, 1987, 356) with trityl chloride in pyridine.

B. Example of Modified Procedure for the Synthesis of Ar_2PCl

Di-[(3,5-bis-trifluoromethyl)-phenyl]chlorophosphine. A 1.0 M solution of (3,5-bis-trifluoromethyl)phenylmagnesium bromide was prepared by slow addition of 18.5 g (60 mmol) of (3,5-bis-trifluoromethyl)bromobenzene in 40 mL of THF to a slurry of Mg turnings in 20 mL of THF. After 1 h, this solution was added slowly to a solution of 5.0 g (29 mmol) of Et_2NPCl_2 in 30 mL of THF at 0°C. After 2 h, the mixture was concentrated in vacuo. Cyclohexane (100 mL) was added and the mixture was filtered through celite to provide a solution of [di-3,5-bis(trifluoromethyl)phenyl](diethyl-amino)phosphine. Dry HCl was passed through this solution for 1 h. After filtration under a nitrogen atmosphere (in some instances, it was necessary to degas the solution to precipitate the amine hydrochloride) and concentration, 12.4 g (88%) of 1a was collected as a white solid. ^{31}P NMR δ 69.8; ^1H NMR δ 7.66 (m, 4) 7.52 (s, 2).

Bis-(4-methoxyphenyl)chlorophosphine. ^{31}P NMR δ 85.4; ^1H NMR δ 7.54 (m, 4), 6.65 (m, 4), 3.17 (s, 6); ^{13}C δ 134.0 (d, 1, J_{PC} = 26 Hz), 128.4 (d, 1, J_{PC} = 24 Hz), 128.2 (d, 1, J_{PC} = 24 Hz), 114.6 (d, 1, J_{PC} = 8 Hz), 54.8.

Bis-(3,5-dimethylphenyl)chlorophosphine. ^{31}P NMR d 85.3; ^1H NMR d 7.25 (m, 4), 6.62 (s, 2), 1.85 (m, 12).

Bis-(3,5-difluorophenyl)chlorophosphine. ^{31}P NMR δ 75.3; ^1H NMR δ 6.93 (m, 4), 6.43 (m, 2).

Bis-(3,5-dimethyl-4-methoxyphenyl)chlorophosphine. ^{31}P NMR δ 89.2; ^1H NMR δ 7.42 (d, 4, J = 12 Hz), 3.18 (s, 6), 1.98 (s, 12).

Bis-(4-fluorophenyl)chlorophosphine. ^{31}P NMR δ 80.6; ^1H NMR δ 7.12 (m, 4), 6.58 (m, 4).

Bis-(4-trifluoromethylphenyl)chlorophosphine. ^{31}P NMR δ 76.3; ^{1}H NMR δ 7.33 (m, 8).

C. Synthesis of Phosphinites

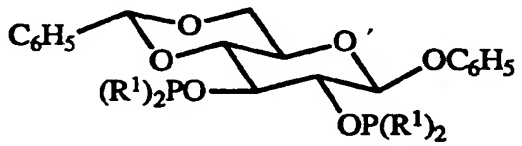
The ligands were synthesized according to methods previously reported in U.S. Patent 5,175,335 (Casalnuovo, A. L.; RajanBabu, T. V.) and the reference, Selke, R.; Pracejus, H. *J. Mol. Catal.* **1986,** *37,* 213.

D. Synthesis of Metal Catalysts

In a dry box under nitrogen, a solution of 0.49 mmols of $Rh(COD)_2^+ X^-$ (X = SbF_6, BF_4, OSO_2CF_3) in 5 mL of CH_2Cl_2 was added to 0.50 mmol of phosphinite in 5 mL of CH_2Cl_2 at room temperature. The mixture was stirred for 30 min to 3 h and the solvent was carefully removed under vacuum. A fine powder of the Rh-complex may be obtained by redissolving the complex in 8 mL of benzene and freeze-drying the sample under high vacuum.

The following ligands and the corresponding catalysts were prepared according to general procedures (A-D) outlined earlier and the structures were confirmed by ^{1}H NMR and ^{31}P NMR.

I. Ligands and catalysts from phenyl 4,6-O-benzylidene-β-D-glucopyranoside



IA. (2,3-diphenylphosphinite), R^1 = Ph (see U.S. Patent 5,175,335, and Selke, R.; Pracejus, H. *J. Mol. Catal.* **1986,** *37,* 213 for ligand synthesis): [IA]Rh(COD)SbF_6 ^{31}P NMR($CDCl_3$): ABX (= P_1P_2Rh), n_a = 137.5, n_b = 138.6, J_{AB} = 27 Hz, J_{AX} = J_{BX} (= J_{RhP}) = 176 Hz; [IA]Rh(COD)BF_4 ^{31}P NMR: ABX (= P_1P_2Rh), η_A = 136.5, η_B = 138.0, JAB = 27 Hz, JAX = JBX (= J_{RhP}) = 178 Hz.

Iridium Catalyst [IA]Ir(COD)BF_4 ^{31}P NMR: 118.6 (d, 1, J_{pp} = 28 Hz), 120.0 (d, 1, J_{pp} = 28 Hz).

IB. (Di-(bis-3,5-dimethylphenyl)phosphinite), $R^1 = 3,5\text{-}(CH_3)_2C_6H_3$ (for ligand see: U.S. Patent 5,175,335): [IB]Rh(COD)SbF_6 ^{31}P NMR($CDCl_3$): ABX (= P_1P_2Rh), $n_a = 136.6$, $n_b = 136.8$, $J_{AB} = 27$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 177 Hz; in C_6D_6 ABX (= P_1P_2Rh), $\eta_A = 134.0$, $\eta_B = 136.0$, $J_{AB} = 29$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 178 Hz.

IC. (Di-(4-methoxyphenyl)phosphinite), $R^1 = 4\text{-}MeO\text{-}C_6H_4$: **IC.** ^1H NMR 3.12 (s, 3 H), 3.17 (s, 3 H), 3.18 (s, 3 H), 3.20 (s, 3 H), 3.29 (t, J = 10, 1 H), 3.54 (t, 10, 1 H), 3.92 (dd, J = 10, 4, 1 H), (4.51 - 4.55 (2 X dd, 2 H), 4.58 (s, 1 H), 4.59 (d, J = 8 Hz), 6.50-7.60 (m, aromatic); ^{31}P 116.59 (d, J = 3, 1 P), 121.06 (d, J = 3, 1 P). [IC]Rh(COD)SbF_6 ^{31}P NMR (C_6D_6) ABX (= P_1P_2Rh), $n_a = 139.5$, $n_b = 140.1$, $J_{AB} = 24$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 182 Hz.; [IC]Rh(COD)OTf ^{31}P NMR (C_6D_6) ABX (= P_1P_2Rh), $\eta_A = 136.8$, $\eta_B = 138.5$, $J_{AB} = 28$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 181 Hz.

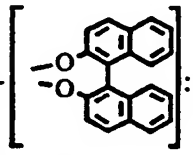
ID. (Di-(4-fluorophenyl)phosphinite), $R^1 = 4\text{-}F\text{-}C_6H_4$: ^1H NMR δ 7.35-6.40 (m, 26), 4.82 (d, 1, J = 8 Hz), 4.80 (s, 1), 4.42 (m, 2), 3.91 (dd,1 J = 5, 10 Hz), 3.28 (m, 2), 3.11 (m, 1); ^{31}P NMR δ 118.0, 114.8. [ID]Rh(COD)SbF_6 ^{31}P NMR($CDCl_3$): multiplet superimposed on an ABX 8-line pattern with further small coupling presumably due to long range interaction with fluorines. d126.5, 126.8, 128.0, 128.3, 129.2, 129.5, 130.8, 131.1.

IE. (Di-(3,5-difluorophenyl)phosphinite), $R^1 = 3,5\text{-}F_2C_6H_3$ (for ligand, see U.S. Patent 5,175,335). [IE]Rh(COD)SbF_6 ^{31}P NMR($CDCl_3$): ABX (= P_1P_2Rh), $\eta_A = 134.7$, $\eta_B = 137.9$, $J_{AB} = 28$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 182 Hz.

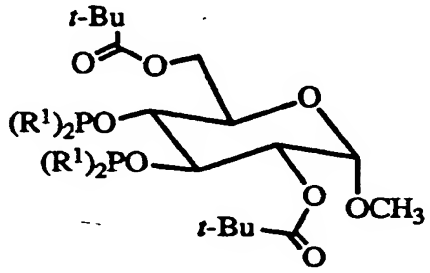
IF. (Di-(bis-3,5-trifluoromethylphenyl)phosphinite), $R^1 = 3,5\text{-}(CF_3)_2C_6H_3$ (for ligand, see U.S. Patent 5,175,335). [IF]Rh(COD)SbF_6 ^{31}P NMR(C_6D_6): ABX (= P_1P_2Rh), $\eta_A = 126.8$, $\eta_B = 130.5$, $J_{AB} = 36$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 182 Hz.

IG. (Di-(4-trifluoromethylphenyl)phosphinite), $R^1 = 4\text{-}CF_3C_6H_4$: ^1H NMR (C_6D_6) 3.05(m, 1 H), 3.10-3.20 (m, 2 H), 3.90 (dd, J = 10, 6, 1 H), 4.36 (m, 2 H), 4.71 (s, 1 H), 4.78 (d, J = 7 Hz, 1 H), 6.28 (d, J = 7 Hz, 1 H), 6.60-7.40

(m, aromatic); ^{31}P 113.0, 115.7; [IG]Rh(COD)BF_4 ^{31}P NMR(C_6D_6): 125.0 (JPP = 36, 1 P), 117.3 (J_{PP} = 36 Hz, 1 P), J_{RhP} = 173 Hz.

IJ. (([R]-2,2'-O-Binapthyl)phosphite), R^1, R^1= (R)-  : (for ligand, see U.S. Patent 5,175,335). [IJ]Rh(COD)BF_4 ^{31}P NMR(C_6D_6): ABX (= P_1P_2Rh), η_A = 132.7, η_B = 138.7, J_{AB} = (=JPP) = 55 Hz, J_{AX} = J_{BX} (= J_{RhP}) = 255 Hz.

II. Ligands and catalysts from Methyl-2,6-O-bis-(trimethyacetyl)-α-D-glucopyranoside



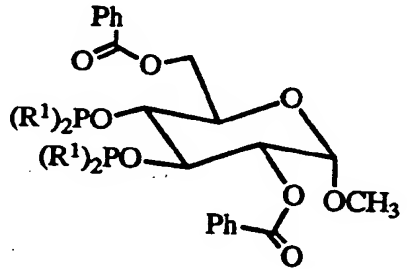
IIA. (3,4-diphenylphosphinite), R^1 = Ph: ^1H NMR δ 7.50-6.78 (m, 20), 5.25 (dd, 1, J = 4, 10 Hz), 5.05 (m, 1), 5.00 (d, 1, J = 3 Hz), 4.44 (m, 1), 4.17 (dd, 1, J = 2, 12 Hz), 3.94 (ddd, 1, J = 2, 5, 10 Hz), 3.75 (dd, 1, J = 5, 12 Hz), 2.97 (s, 3), 1.14 (s, 9) 0.93 (s, 9); ^{31}P NMR δ 118.0 (d, 1, J_{pp} = 5 Hz), 114.8 (d, 1, J_{pp} = 5 Hz); [IIA]Rh(COD)BF_4 ^{31}P NMR(C_6D_6): ABX (= P_1P_2Rh), η_A = 134.0, η_B = 136.5, J_{AB} = 30 Hz, J_{AX} = J_{BX} (= J_{RhP}) = 178 Hz.

IIB. (3,4-Di-(bis-3,5-dimethylphenyl)phosphinite), R^1 = 3,5-$(CH_3)_2C_6H_3$: ^1H NMR δ 7.35-7.18 (m, 6), 6.95-6.85 (m, 2), 6.64 (s, 1), 6.53 (s, 1), 6.47 (s, 1), 6.33 (s, 1), 5.30 (m, 1), 5.08 (m, 1), 4.89 (m, 1), 4.50 (m, 1), 4.12 (dm, 1, J = 12 Hz), 3.95 (m, 1), 3.72 (m, 1), 2.88 (s, 3), 1.99 (s, 6), 1.98 (s, 6), 1.93 (s, 6), 1.90 (s, 6); ^{31}P NMR δ 122.1, 117.9; [IIB]Rh(COD)BF_4 ^{31}P NMR(C_6D_6): ABX (= P_1P_2Rh), η_A = 129.0, η_B = 135.2, J_{AB} = 30 Hz, J_{AX} = J_{BX} (= J_{RhP}) = 176.

IIF. (3,4-Di-(bis-3,5-trifluoromethylphenyl)phosphinite), R^1 = 3,5-$(CF_3)_2C_6H_3$: ^1H NMR δ 8.01-6.63 (m, 12), 5.02 (dd, 1, J = 4, 10 Hz), 4.86 (m, 1), 4.83 (d, 1, J = 4 Hz), 4.06 (m, 1), 3.86 (m, 2), 3.65 (dd, 1, J = 6, 12 Hz), 2.90 (s, 3), 1.01 (s, 9), 0.85 (s, 9); ^{31}P NMR δ 111.9, 105.7.; [IIF]Rh(COD)BF_4 In addition to the eight line pattern at 125.3, 125.7, 126.1, 126.4, 127.2, 127.6, 127.9 there is another set of broad doublets which appear around δ 130, 132, 141 and 143.

IIH. (3,4-Di-{(bis-3,5-dimethyl)-4-O-methyl-phenyl}phosphinite), R^1 = 3,5-$(CH_3)_2$-4-(CH_3O)-C_6H_2: ^1H NMR δ 7.39 (m, 4), 7.30 (m, 2), 7.09 (m, 2), 5.39 (dd, 1, J = 4, 10 Hz), 5.19 (m, 1), 4.97 (d, 1, J = 4 Hz), 4.57 (m, 1), 4.12 (dd, 1, J = 1, 12 Hz), 4.04 (ddd, 1, J = 1, 4, 10 Hz), 3.77 (dd, 1, J = 5, 12 Hz), 3.38 (m, 3), 3.28 (m, 3), 3.22 (s, 3), 3.14 (s, 3), 2.95 (s, 3), 2.17 (s, 3), 2.12 (s, 6), 2.11 (s, 3), 1.16 (s, 9), 0.96 (s, 9); ^{31}P NMR δ 123.2 (d, 1, J_{pp} = 3 Hz), 117.8 (d, 1, J_{pp} = 3 Hz). [IIH]Rh(COD)BF_4 ^{31}P NMR(C_6D_6): ABX (= P_1P_2Rh), η_A = 129.3, η_B = 135.6, J_{AB} = 30 Hz, J_{AX} = J_{BX} (= J_{RhP}) = 176 Hz.

III. Ligands and catalysts from methyl 2,6-O-dibenzoyl-α-D-glucopyranoside



IIIA. (3,4-diphenylphosphinite), R^1 = Ph: ^1H NMR δ 8.12 (m, 2), 7.85 (m, 2), 7.50-6.49 (m, 16), 5.40 (dd, 1, J = 4, 12 Hz), 5.22 (m, 1), 5.08 (d, 1, J = 3 Hz), 4.70 (m, 1), 4.39 (d, 1, J = 12 Hz), 4.04 (dd, 1, J = 4, 10 Hz), 3.91 (dd, 1, J = 4, 12 Hz), 2.78 (s, 3); ^{31}P NMR δ 120.0 (d, 1, J_{pp} = 4 Hz), 116.0 (d, 1, J_{pp} = 4 Hz). [IIIA]Rh(COD)BF_4 NMR(C_6D_6): ABX (= P_1P_2Rh), η_A = 130.8, η_B = 133.7, J_{AB} = 32 Hz, J_{AX} = J_{BX} (= J_{RhP}) = 176 Hz.

IIIB. (3,4-Di-(bis-3,5-dimethylphenyl)phosphinite), $R^1 = 3,5\text{-}(CH_3)_2C_6H_3$: ^1H NMR δ 8.13 (m, 2), 7.80 (m, 2), 7.30-6.70 (m, 14), 6.63 (s, 1), 6.46 (s, 1), 6.32 (s, 1), 6.03 (s, 1), 5.51 (dd, 1, J = 4, 10 Hz), 5.23 (m, 1), 5.00 (d, 1, J = 3 Hz), 4.89 (m, 1), 4.42 (d, 1, J = 12 Hz), 4.04 (dd, 1, J = 4, 10 Hz), 3.90 (dd, 1, J = 4, 12 Hz), 2.75 (s, 3), 2.02 (s, 6), 1.91 (s, 6),1.88 (s, 6), 1.73 (s, 6); ^{31}P NMR δ 124.7, 118.8. [IIIB]Rh(COD)BF_4 NMR(C_6D_6): ABX (= P_1P_2Rh), $\eta_A = 129.0$, $\eta_B = 130.4$, $J_{AB} = 10$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 175 Hz; [IIIA]Rh(COD)SbF_6 NMR(C_6D_6): ABX (= P_1P_2Rh), $\eta_A = 132.8$, $\eta_B = 134.2$, $J_{AB} = 30$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 151 Hz.

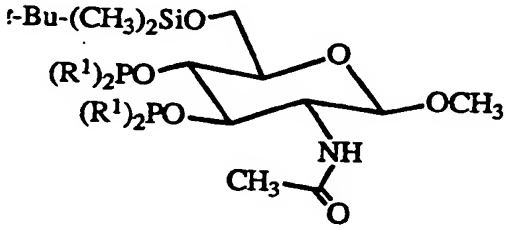
IIIC. (3,4-Di-(4-methoxyphenyl)phosphinite), $R^1 = 4\text{-}(CH_3O)C_6H_4$: ^1H NMR δ 8.40-6.46 (m, 26), 5.69 (dd, 1, J = 4, 10 Hz), 5.45 (m, 1), 5.27 (d, 1, J = 4 Hz), 4.93 (m, 1), 4.65 (dd, 1, J = 2, 12 Hz), 4.29 (m, 1), 4.19 (m, 1), 3.41 (s, 3), 3.34 (s, 3), 3.32 (s, 3), 3.19 (s, 3), 3.02 (s, 3); ^{31}P NMR δ 120.5 (d, 1, $J_{pp} = 5$ Hz), 117.8 (d, 1, $J_{pp} = 5$ Hz). [IIIC]Rh(COD)BF4 NMR(C_6D_6): ABX (= P_1P_2Rh), $\eta_A = 134.4$, $\eta_B = 136.1$, $J_{AB} = 28$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 181 Hz.

[IIIE]Rh(COD)BF_4 NMR(C_6D_6): ABX (= P_1P_2Rh), $\eta_A = 126.7$, $\eta_B = 127.6$, $J_{AB} = 39$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 179 Hz.

IIIF. (3,4-Di-(bis-3,5-trifluoromethylphenyl)phosphinite), $R^1 = 3,5\text{-}(CF_3)_2C_6H_3$: ^1H NMR δ 8.22-6.89 (m, 32), 5.45 (dd, 1, J = 4, 10 Hz), 5.19 (m, 1), 5.11 (d, 1, J = 4 HZ), 4.52 (m, 1), 4.28 (d, 1, J = 12 Hz), 4.11 (dd, 1, J = 5, 10 Hz), 3.98 (dd, 1, J = 5 12 Hz), 2.93 (s, 3); ^{31}P NMR δ 113.0, 107.5.

IIIG. (3,4-Di-(4-trifluoromethylphenyl)phosphinite), $R^1 = 4\text{-}CF_3C_6H3$ ^1H NMR(C_6D_6) 2.80 (s, 3 H), 3.85 (dd, J = 13, 4, 1 H), 4.06 (ddm, J = 8, 4, 1 H), 4.28 (dd, J = 13, 2, 1 H), 4.60 (dt, J = 12, 12 1 H), 5.00 (m, 1 H), 5.03 (d, J = 4, 1 H), 5.28 (dd, 12, 4, 1 H), 6.70-7.60 (m, aromatic); [IIIG]Rh(COD)BF_4 NMR(C_6D_6): ABX (= P_1P_2Rh), $\eta_A = 125.2$, $\eta_B = 127.4$, $J_{AB} = 37$ Hz, $J_{AX} = J_{BX}$ (= J_{RhP}) = 177 Hz.

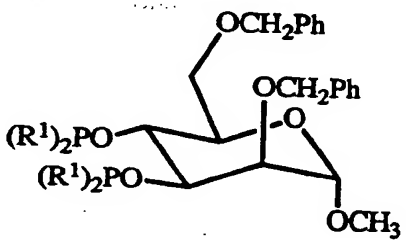
IV. Ligands and catalysts from methyl-2-acetamido-6-O-(*t*-butyldimethylsilyl)-2-deoxy-β-D-glucopyranoside



IVA. (3,4-diphenylphosphinite), R^1 = Ph Ligand: ^{31}P NMR (C_6D_6) 112.70 (d, J_{PP} = 5 Hz), 117.17 (d, J_{PP} = 5 Hz); [IVA]$RhSbF_6$ (C_6D_6) ABX (= PPRh), η_A = 122.5, η_B = 129.2, J_{AB} (JPP) = 35, J_{RhP} = 173.

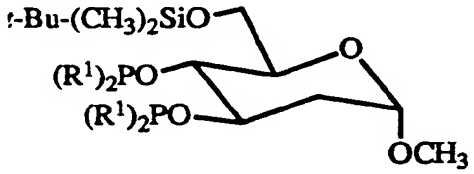
IVB. (3,4-Di-(bis-3,5-dimethylphenyl)phosphinite), R^1 = 3,5-$(CH_3)_2C_6H_3$: ^1H NMR δ 7.55-7.22 (m, 8), 6.86 (s, 1), 6.72 (s, 1), 6.64 (s, 1), 6.59 (s, 1), 5.26 (m, 1), 5.13 (d, 1, J = 8 Hz), 4.73 (m, 2), 4.42 (m, 1), 3.80 (m, 3), 3.49 (s, 3), 2.20 (s, 15), 2.17 (s, 6), 2.11 (s, 6), 1.12 (s, 9), 0.16 (s, 3), 0.15 (s, 3); ^{31}P NMR δ 120.4 (d, 1, J_{pp} = 4 Hz), 115.7 (d, 1, J_{pp} = 4 Hz); [IVB]$RhBF_4$ (C_6D_6) ABX (= PPRh), η_A = 118.9, η_B = 126.6, J_{AB} (JPP) = 34, J_{RhP} = 170.

V. Ligands and catalysts from methyl-2,6-O-dibenzyl-α-D-mannopyranoside



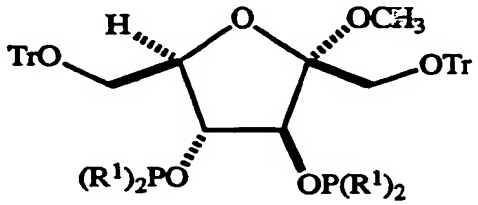
VA. (3,4-diphenylphosphinite), R^1 = Ph: ^1H NMR δ 7.78-6.80 (m, 20), 5.09 (m, 1), 4.95 (m, 1), 4.72 (d, 1, J = 2, Hz), 4.22 (m, 4), 4.11 (m, 1), 4.02 (m, 1), 3.55 (m, 2), 3.13 (s, 3); ^{31}P NMR δ 117.3, 110.4; [VA]$Rh(COD)BF_4$ (C_6D_6) ^{31}P: η_A = 129.2, η_B = 137.2, J_{PP} = 27, J_{RhP} = 177; [VB]$Rh(COD)BF_4$(C_6D_6) ^{31}P: η_A = 124.8, η_B = 133.9, J_{pp} = 30; $J_{Rh,P}$ = 176.

VI. Ligands and catalysts from methyl-6-O-(*t*-butyldimethylsilyl)-2-deoxy-α-D-glucopyranoside



VIB. (3,4-Di-(bis-3,5-dimethylphenyl)phosphinite), R^1 =3,5-$(CH_3)_2C_6H_3$: ^1H NMR δ 7.61-7.26 (m, 8), 6.88 (s, 1), 6.81 (s, 1), 6.65 (s, 1), 6.60 (s, 1), 5.20 (m, 1), 4.64 (m, 1), 4.45 (d, 1, J = 3 Hz), 3.14 (s, 3), 2.21 (s, 6), 2.16 (s, 6), 2.14 (s, 6), 2.12 (s, 6), 1.11 (s, 9), 0.11 (s, 3), 0.11 (s, 3); ^{31}P NMR δ 121.1 (d, 1 J_{pp} = 2 Hz), 113.1 (d, 1, J_{pp} = 2 Hz); [VIB]Rh OTf (C_6D_6) ABX (= PPRh), η_A = 123.6, η_B = 128.2, J_{AB} (JPP) = 34, J_{RhP} = 173. [VIB]Ph(COD)BF_4 $^{31}P(C_6D_6)$ ABX (=PPRh) η_A = 124.9, η_B = 127.4, J_{AB} = 33, $J_{Rh,P}$ = 173.

VII. Ligands and catalysts from methyl-5,6-O-triphenylmethyl-α-D-fructofuranoside



Tr = triphenylmethyl

VIIA. (3,4-diphenylphosphinite), R^1 = Ph: ^1H NMR (C_6D_6) 3.10 (s, 3H), 3.35, 3.45 (ABX, J_{AB} = 10, J_{AX} = 7, J_{BX} = 6, 2 H), 3.60, 3.78 (AB, J_{AB} = 10, 2 H), 4.50 (ddm, br, 1H), 4.88 (m, 1H), 5.00 (d, J = 10, 1 H), 6.80-7.80 (m, aromatic); ^{31}P NMR (C_6D_6) 114.2, 115.1 (AB, J_{PP} = 9). [VIIA]$RhSbF_6$ (C_6D_6) ABX (= PPRh), η_A = 119.7, η_B = 122.8 J_{AB} (J_{PP}) = 29, J_{RhP} = 166.

VIIB. (3,4-Di-(bis-3,5-dimethylphenyl)phosphinite), R^1 =3,5-$(CH_3)_2C_6H_3$: ^1H NMR δ 1.85, 1.91, 1.94, 2.05 (4Xs, 3H each), 3.10 (s, 3H), 3.45-3.60 (ABX, J_{AB} = 9, J_{AX} = J_{BX} = 5, 2H), 3.67, 3.80 (ABq, JAB = 10, 2H), 4.47 (qm, br, 1H), 5.63 (d, J = 11 Hz, 1 H), 5.20 (m, 1 H), 6.50-7.80 (m, aromatic); ^{31}P NMR (C_6D_6) δ 116.41(d, J_{PP} = 8, 1 P), 118.53(d, J_{PP} = 8, 1 P).

[VIIB]Rh(COD)BF_4: ^{31}P NMR(C_6D_6): 114.2 (dd, J_{RhP} = 169, J_{PP} = 28, 1 P), 131.5 (dd, J_{RhP} = 169, J_{PP} = 28, 1 P).

VIIC. (3,4-Di-(4-methoxyphenyl)phosphinite), R^1 = 4-(CH_3O)C_6H_4: ^1H NMR (C_6D_6) 3.05-3.30 (4Xs total 15 H), 3.40, 3.50 (ABX, J_{AB} = 10, J_{AX} = 7, J_{BX} = 6, 2 H), 3.61, 3.79 (AB, J_{AB} = 10, 2 H), 4.58 (ddm, br, 1H), 4.90 (m, 1H), 5.05 (d, J = 10, 1 H), 6.42-7.61 (m, aromatic); ^{31}P NMR (C_6D_6) 115.0, 115.2 (AB, J_{PP} = 7). [VIIC]Rh(COD)SbF_6 (C_6D_6) ABX (= PPRh), n_A = 121.8, n_B = 122.1, J_{AB} (= J_{PP}) = 27, J_{RhP} = 167; [VIIC]Rh(COD)OTf (C_6D_6) ABX (= PPRh), η_A = 121.3, η_B = 121.9, J_{AB} (= J_{PP}) = 28, J_{RhP} = 166.

VIII. Ligands and catalysts from 2-naphthyl 4,6-O-benzylidene-β-D-glucopyranoside

VIIIA. (2,3-diphenylphosphinite), R^1 = Ph: ^1H NMR 3.25 (dt, J = 8, 4, 1 H), 3.35 (t, J = 9, 1 H), 3.51 (t, J = 9, 1 H), 4.00 (dd, J = 8, 4, 1 H), 4.40-4.60 (m, 2 H), 4.85 (s, 1 H), 5.02 (d, J = 8, 1 H), 6. 50-7.52 (m, aromatic). [VIIIA]Rh(COD)SbF_6 ^{31}P NMR($CDCl_3$): ABX (= P_1P_2Rh), η_A = 137.9, η_B = 139.2, J_{AB} = 21 Hz, J_{AX} = J_{BX} (= J_{RhP}) = 192 Hz

Asymmetric Hydrogenation Reactions:

General Procedure for Scouting Reactions. In the dry box, a 150 mL Fisher-Porter tube was charged with 50 mg of acetamidoacrylate derivative, 1 mg of L*Rh(COD)A, and 1 mL of solvent (THF, MeOH, DME, etc.). The tube was sealed and charged with H_2 (10-100 psi). After 3 h, the tube was vented. When Z^3 = CH_3, the crude product was analyzed directly by GC (25 m x 0.25 mm Chiralsil L-VAL capillary column) for enantiomeric excess determination. In the case of Z^3 = H, the crude product was treated with diazomethane prior to analysis by GC. Pure samples of the amino acid derivatives were obtained by recrystallization or by flash chromatography and characterized by ^1H NMR.

Synthesis of D-amino acid derivatives (R-configuration)

Examples 1-56 provide D-amino acids under the hydrogenation conditions desribed above.

Table 1

Hydrogenation of Dehydroamino Acid Derivatives

$[Z^1Z^2C=C(CO_2Z^3)(NHZ^4)$, $Z^1 = H$, $Z^4 = Ac]$ Using L*Rh(COD)A[a]

Ex.	Cat.	Z^2	Z^3	% ee (R-)	Conditions[a]
1	[IIA]Rh(COD)BF_4	C_6H_5	CH_3	80.2	
2	[IIA]Rh(COD)BF_4	C_6H_5	CH_3	84	run at -10°C
3	[IIB]Rh(COD)BF_4	C_6H_5	CH_3	92.4	
4	[IIB]Rh(COD)BF_4	C_6H_5	CH_3	94.5	run at -10°C
5	[IIF]Rh(COD)BF_4	C_6H_5	CH_3	11	
6	[IIH]Rh(COD)BF_4	C_6H_5	CH_3	93.1	
7	[IIA]Rh(COD)BF_4	C_6H_5	CH_3	39.8	run in MeOH
8	[IIB]Rh(COD)BF_4	C_6H_5	CH_3	91.4	run in DME
9	[IIB]Rh(COD)BF_4	C_6H_5	CH_3	88.1	run in Toluene
10	[IIB]Rh(COD)BF_4	C_6H_5	CH_3	87.6	run in Bu_2O
11	[IIB]Rh(COD)BF_4	C_6H_5	CH_3	76.4	run in EtOH
12	[IIB]Rh(COD)BF_4	C_6H_5	CH_3	74.5	run in MeOH
13	[IIH]Rh(COD)BF_4	C_6H_5	CH_3	88.4	run in Bu_2O
14	[IIH]Rh(COD)BF_4	C_6H_5	CH_3	88.2	run in Toulene
15	[IIH]Rh(COD)BF_4	C_6H_5	CH_3	92.4	run in DME
16	[IIH]Rh(COD)BF_4	C_6H_5	CH_3	80.0	run in EtOH
17	[IIH]Rh(COD)BF_4	C_6H_5	CH_3	79.0	run in MeOH
18	[IIB]Rh(COD)BF_4	C_6H_5	H	94.5	
19	[IIB]Rh(COD)BF_4	4-FC_6H_4	CH_3	92.0	
20	[IIB]Rh(COD)BF_4	3-(MeO)C_6H_4	CH_3	93.1	
21	[IIB]Rh(COD)BF_4	2-Napth	CH_3	92.0	
22	[IIB]Rh(COD)BF_4	2-Napth	H	93.0	
23	[IIIA]Rh(COD)BF_4	C_6H_5	CH_3	58.7	
24	[IIIB]Rh(COD)BF_4	C_6H_5	CH_3	93.0	
25	[IIIC]Rh(COD)BF_4	C_6H_5	CH_3	84.7	
26	[IIIE]Rh(COD)BF_4	C_6H_5	CH_3	1.0	
27	[IIIF]Rh(COD)BF_4	C_6H_5	CH_3	2.3	
28	[IIIG]Rh(COD)BF_4	C_6H_5	CH_3	2.0	
29	[IIIB]Rh(COD)SbF_6	C_6H_5	CH_3	96.0	
30	[IIIB]Rh(COD)BF_4	C_6H_5	CH_3	94.0	run in DME
31	[IIIB]Rh(COD)BF_4	C_6H_5	CH_3	77.9	run in MeOH

32	[IIIB]Rh(COD)BF_4	C_6H_5	CH_3	87.6	run in Toluene
33	[IIIB]Rh(COD)BF_4	C_6H_5	H	95.8	
34	[IIIB]Rh(COD)SbF_6	C_6H_5	H	97.0	
35	[IIIB]Rh(COD)SbF_6	4-FC_6H_4	CH_3	96.2	
36	[IIIB]Rh(COD)BF_4	4-FC_6H_4	CH_3	80.2	run in MeOH
37[b]	[IIIB]Rh(COD)SbF_6	4-FC_6H_4	CH_3	90[c]	
38	[IIIB]Rh(COD)BF_4	4-FC_6H_4	H	95.4	
39	[IIIB]Rh(COD)SbF_6	4-FC_6H_4	H	96.4	
40	[IIIB]Rh(COD)SbF_6	$(CH_3)_2CH$	H	89.2	
41	[IIIB]Rh(COD)SbF_6	3-thienyl	CH_3	97.0	
42	[IVA]Rh(COD)BF_4	C_6H_5	CH_3	94.9	
43	[IVB]Rh(COD)BF_4	C_6H_5	CH_3	98.3	
44	[IVA]Rh(COD)BF_4	C_6H_5	H	94.5	
45	[IVB]Rh(COD)BF_4	C_6H_5	H	94.5	
46	[IVB]Rh(COD)BF_4	4-FC_6H_4	CH_3	97.8	
47	[VA]Rh(COD)BF_4	C_6H_5	CH_3	55.4	
48	[VA]Rh(COD)BF_4	C_6H_5	CH_3	18.1	run in MeOH
49	[VB]Rh(COD)BF_4	C_6H_5	CH_3	72.2	
50	[VIB]Rh(COD)OTf	C_6H_5	CH_3	76.0	
51	[VIB]Rh(COD)BF_4	C_6H_5	CH_3	65.1	
52	[VIIA]Rh(COD)SbF_6	C_6H_5	CH_3	48.0	
53	[VIIC]Rh(COD)SbF_6	C_6H_5	CH_3	51	
54	[VIIA]Rh(COD)SbF_6	C_6H_5	H	51.0	
55	[VIIA]Rh(COD)SbF_6	4-FC_6H_4	CH_3	53.0	
56	[VIIB]Rh(COD)BF_4	4-FC_6H_4	CH_3	56.8	
57	[VIIC]Rh(COD)SbF_6	4-FC_6H_4	CH_3	57.0	

[a]Reaction performed at ambient temperature in THF under 40 psi of H_2 pressure unless noted.
[b]In this case, Z^4 = C(O)OCH_2Ph (Cbz).
[c]EE determined on alcohol after reduction of crude product with $LiBH_4$.

Synthesis of L-amino acid derivatives (S-configuration)

Examples 57-98 provide L-amino acids under the hydrogenation conditions desribed above.

Table 2

Hydrogenation of Dehydroamino Acid Derivatives

[$Z^1Z^2C=C(CO_2Z^3)(NHZ^4)$, Z^1 = H, Z^4 = Ac] Using L*Rh(COD)A[a]

Ex.	Cat.	Z^2	Z^3	% ee (S-)	Remarks[a]
57	[IB]Rh(COD)SbF_6	C_6H_5	CH_3	96	
58	[IE]Rh(COD)SbF_6	C_6H_5	CH_3	2.0	
59	[IG]Rh(COD)BF_4	C_6H_5	CH_3	9.8	
60	[IA]Rh(COD)SbF_6	C_6H_5	H	94.0	
61	[IB]Rh(COD)SbF_6	C_6H_5	H	99	
62	[IC]Rh(COD)SbF_6	C_6H_5	H	93.0	
63	[IC]Rh(COD)OTf	C_6H_5	H	96.0	
64	[ID]Rh(COD)SbF_6	C_6H_5	H	91	
65	[IE]Rh(COD)SbF_6	C_6H_5	H	60	
66	[IF]Rh(COD)SbF_6	C_6H_5	H	71	
67	[IJ]Rh(COD)SbF_6	C_6H_5	H	47.0	
68	[IA]Rh(COD)SbF_6	4-FC_6H_4	CH_3	84.0	
69	[IA]Rh(COD)BF_4	4-FC_6H_4	CH_3	85.0	
70	[IB]Rh(COD)SbF_6	4-FC_6H_4	CH_3	97.2	
71	[IC]Rh(COD)SbF_6	4-FC_6H_4	CH_3	89	
72	[ID]Rh(COD)SbF_6	4-FC_6H_4	CH_3	81.0	
73	[IE]Rh(COD)SbF_6	4-FC_6H_4	CH_3	13	
74	[IF]Rh(COD)SbF_6	4-FC_6H_4	CH_3	9	
75	[IB]Rh(COD)SbF_6	4-FC_6H_4	CH_3	96.7	run in EtOH
76	[IB]Rh(COD)SbF_6	4-FC_6H_4	H	98.0	
77[b]	[IA]Rh(COD)SbF_6	4-FC_6H_4	CH_3	62[c]	
78[b]	[IB]Rh(COD)SbF_6	4-FC_6H_4	CH_3	97.0[c]	
79[b]	[IC]Rh(COD)SbF_6	4-FC_6H_4	CH_3	85.0[c]	
80[b]	[IF]Rh(COD)SbF_6	4-FC_6H_4	CH_3	54[c]	
81	[IB]Rh(COD)SbF_6	3-(MeO)C_6H_4	CH_3	98.1	
82	[IE]Rh(COD)SbF_6	3-(MeO)C_6H_4	CH_3	21.0	
83	[IA]Rh(COD)SbF_6	3-(MeO)C_6H_4	H	91	
84	[IB]Rh(COD)SbF_6	3-(MeO)C_6H_4	H	97.0	
85	[IE]Rh(COD)SbF_6	3-(MeO)C_6H_4	H	53.0	
86	[IF]Rh(COD)SbF_6	3-(MeO)C_6H_4	H	5	
87	[IA]Rh(COD)BF_4	2-Napth	H	94.2	

88	[IB]Rh(COD)SbF_6	2-Napth	H	97.9
89	[IB]Rh(COD)SbF_6	4-BrC_6H_4	H	98
90	[IE]Rh(COD)SbF_6	4-BrC_6H_4	H	47
91	[IA]Rh(COD)SbF_6	$(CH_3)_2CH$	H	90.0
92	[IB]Rh(COD)SbF_6	$(CH_3)_2CH$	H	91.0
93	[IC]Rh(COD)SbF_6	$(CH_3)_2CH$	H	83.3
94	[IF]Rh(COD)SbF_6	$(CH_3)_2CH$	H	26.0
95	[IA]Rh(COD)SbF_6	3-thienyl	CH_3	86.6
96	[IB]Rh(COD)SbF_6	3-thienyl	CH_3	96.7
97	[VIIIA]Rh(COD)SbF_6	C_6H_5	H	89
98	[VIIIA]Rh(COD)SbF_6	3-(MeO)C_6H_4	H	89.0

[a]Reaction performed at ambient temperature in THF under 40 psi of H_2 pressure unless noted.
[b]In this case, Z^4 = C(O)OCH_2Ph (Cbz).
[c]EE determined on alcohol after reduction of crude product with $LiBH_4$.

Hydrogenation using Ir catalyst

A solution of 50 mg (0.23 mmol) of methyl acetamidocinnamte and 1 mg of [IA]Ir(COD)BF_4 in 1 mL of THF was placed in a Fisher-Porter tube in the drybox. This material was charged with 30 psi of H_2 pressure and heated to 100°C. The pressure rose to 50 psi. After 3 h, the tube was vented and analyzed as usual. A 7.7% ee (enriched with S-isomer) was obtained.

WHAT IS CLAIMED IS:

1. A process for asymmetric hydrogenation, comprising:

reacting a dehydroamino acid derivative of formula I

$$ZZC{=}C(CO_2Z)(NHZ)$$

I

wherein each Z is independently H or a C_1 to C_{40} carboalkoxy, C_1 to C_{40} aromatic or nonaromatic hydrocarbyl or C_1 to C_{40} aromatic or nonaromatic heterocyclic radical; optionally substituted with one or more halo, alkoxy, carboalkoxy, nitro, haloalkyl, hydroxy, amido, keto or sulfur containing groups;

with a source of hydrogen;

in the presence of a catalyst composition comprising iridium or rhodium and a chiral, nonracemic diphosphinite ligand of formula II

$$(R^1)_2\text{-P-X-}R^2\text{-X-P-}(R^1)_2$$

II

wherein R^2 is a C_4 to C_{40} dideoxycarbohydrate;

each X is independently O or NR^3, wherein R^3 is H, a C_1 to C_{20} alkyl or aryl; and

each R^1 is independently an aromatic hydrocarbyl substituted with one or more amino, dialkylamino, hydroxy, alkoxy, alkyl, trialkylsilyl, trialkyaryl groups or an aromatic heterocycle substituted with one or more amino, dialkylamino, hydroxy, alkoxy, alkyl, trialkylsilyl, or triarylsilyl groups ;

to yield a chiral, nonracemic mixture of compounds of formula III

$$ZZCH\text{-}CH(CO_2Z)(NHZ)$$

III

wherein Z is defined as above.

2. The process of Claim 1 wherein in formula II, the X groups are attached to R^2 in a Right-Left diphosphinite configuration, whereby the asymmetric hydrogenation process selectively yields compounds of formula III in S-configuration.

3. The process of Claim 1 wherein in formula II, the X groups are attached to R^2 in a Left-Right diphosphinite configuration, whereby the asymmetric hydrogenation process selectively yields compounds of formula III in R-configuration.

4. The process of Claim 1 wherein the catalyst compositions comprises rhodium, and X is O.

5. The process of Claim 1 wherein the dehydroamino acid derivatives of formula I are selected from α-acetamidocinnamic acid and its methyl ester; 2-acetamido-3-(4-fluorophenyl)-prop-2-enoic acid and its methyl ester, 2-acetamido-3-(3-methoxyphenyl)-prop-2-enoic acid and its methyl ester, methyl 2-acetamido-3-(4-trifluoromethylphenyl)-prop-2-enoate, methyl 2-acetamido-3-(4-methoxyphenyl)-prop-2-enoic acid and its methyl ester, methyl 2-acetamido-3-(4-bromophenyl)-prop-2-enoic acid, methyl 2-N-benzyloxycarbonyl-3-(4-fluoro-phenyl)-prop-2-enoate, 2-acetamidoacrylic acid, 2-acetamido-3-isopropylacrylic acid, 2-acetamido-3-(2-naphthyl)prop-2-enoic acid and its methyl ester, and methyl 2-acetamido-3-(3-thienyl)prop-2-enoate.

6. The process of Claim 2 wherein R^2 of formula II is selected from 2,3-dideoxyglucose; 2,3-dideoxyxylose; 2,3-dideoxyarabinose; 2,3-dideoxy-maltose; 2,3-dideoxymannose; 2,3-dideoxyyallose; 2,3-dideoxylactose; or their corresponding amino sugars.

7. The process of Claim 2 wherein the catalyst composition comprises rhodium, R^2 of formula II is 2,3-dideoxyglucopyranose, each X is O and each R^1 is independently an alkyl or alkoxy substituted phenyl.

8. The process of Claim 3 wherein the R^2 of formula II is selected from 3,4-dideoxyglucose; 3,4-dideoxyfructose; 3,4-dideoxymannose; 3,4-dideoxy-xylose; 3,4-dideoxyarabinose; 3,4-dideoxymaltose; 3,4-dideoxylactose; or their corresponding amino sugars.

9. The process of Claim 3 wherein the catalyst composition comprises rhodium, R^2 of formula II is 3,4-dideoxyglucopyranose, each X is O, and each R^1 is independently an alkyl or alkoxy substituted phenyl.

10. A catalyst composition comprising iridium or rhodium and a chiral, nonracemic diphosphinite ligand of formula II

$$(R^1)_2\text{-P-X-}R^2\text{-X-P-}(R^1)_2$$

wherein R^2 is a C_4 to C_{40} dideoxycarbohydrate;

each X is independently O or NR^3, wherein R^3 is H, a C_1 to C_{20} alkyl or aryl; and

each R^1 is independently an aromatic hydrocarbyl substituted with amino, dialkylamino, hydroxy, alkoxy, alkyl or trialkyl silyl groups or an aromatic heterocycle substituted with amino, dialkylamino, hydroxy, alkoxy, alkyl, trialkylsilyl or triarylsilyl groups.

11. The catalyst composition of Claim 10 comprising rhodium.

12. The catalyst composition of Claim 10 wherein each X is O.

13. The catalyst composition of Claim 10 wherein R^2 is selected from 2,3-dideoxyglucose; 2,3-dideoxyxylose; 2,3-dideoxyarabinose; 2,3-dideoxy-maltose; 2,3-dideoxymannose; 2,3-dideoxyyallose; 2,3-dideoxylactose; 3,4-dideoxyglucose; 3,4-dideoxyfructose; 3,4-dideoxymannose; 3,4-dideoxyxylose; 3,4-dideoxyarabinose; 3,4-dideoxymaltose; 3,4-dideoxylactose; or their corresponding amino sugars.

14. The catalyst composition of Claim 10 wherein each R^1 is independently an alkyl or alkoxy substituted phenyl.

15. The catalyst composition of Claim 10 comprising rhodium wherein each X is O, R^2 is 2,3-dideoxyglucopyranose or 3,4-dideoxyglucopyranose, and each R^1 is 3,5-dimethylphenyl.

16. A process for asymmetric hydrogenation, comprising reacting a dehydroamino acid derivative of formula I

$$ZZC{=}C(CO_2Z)(NHZ)$$

I

wherein each Z is independently H or a C_1 to C_{40} carboalkoxy, C_1 to C_{40} aromatic or nonaromatic hydrocarbyl or C_1 to C_{40} aromatic or nonaromatic heterocyclic radical, optionally substituted with one or more halo, alkoxy, carboalkoxy, nitro, haloalkyl, hydroxy, amido, keto or sulfur containing groups;

with a source of hydrogen;

in the presence of a catalyst composition comprising iridium or rhodium and a chiral nonracemic diphosphinite ligand of formula II

$(R^1)_2$-P-X-R^2-X-P-$(R^1)_2$

II

wherein R^2 is a C_4 to C_{40} dideoxycarbohydrate;

each X is independently O or NR^3, wherein R^3 is H, a C_1 to C_{20} alkyl or aryl; and

each R^1 is an unsubstituted aromatic hydrocarbyl to,

yield a chiral, nonracemic mixture of compounds of formula III

ZZCH-CH(CO_2Z)(NHZ)

III

wherein Z is defined as above;

and wherein in formula II the X groups are attached to R^2 in the Left-Right diphosphinite configuration whereby the asymmetric hydrogenation process selectively yields compounds of formula III in R-configuration.

17. The process of Claim 16 wherein each R^1 is phenyl.

INTERNATIONAL SEARCH REPORT

Intern nal Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07C231/18 C07C227/32 C07C233/47 C07D333/24 B01J31/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07C B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL AND PHARMACEUTICAL BULLETIN., vol.40, no.10, 1992, TOKYO JP pages 2894 - 2896 T. MORIMOTO ET AL. 'Effects of the Diarylphophino Groups of Modified DIOPS on the Enantioselectivity and the Catalytic Activity of their Rhodium(I) Complexes in the Catalytic Asymmetric Hydrogenations of Enamides' see the whole document --- -/--	1-17

[X] Further documents are listed in the continuation of box C. [ ] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Inter. ...nal Application No
PCT/US 95/00010

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TETRAHEDRON LETTERS, no.34, 1979, OXFORD GB pages 3163 - 3166 KEN-ICHI ONUMA ET AL. 'Chiral Recognition by various Bisphosphine-Rhodium Complexes in Asymmetric Hydrogenation of Olefins through Helical Conformation of Phenyl Groups on the Phosphorous Atom' ---	1-17
P,X	JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol.116, 4 May 1994, WASHINGTON, DC US pages 4101 - 4102 T. V. RAJANBABU, T. A. ET AL 'Electronic Amplification of Selectivity in Rh-Catalyzed Hydrogenations: D-Glucose-Derived Ligands for the Synthesis of D- or L-Amino Acids' ---	1-17
P,X	TETRAHEDRON LETTERS, vol.35, no.25, 20 June 1994, OXFORD GB pages 4295 - 4298 T. V. RAJANBABU, T. A. AYERS 'Electronic Effects in Asymmetric Catalysis: Hydroformylation of Olefins' -----	10-15

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